Epithelial-mesenchymal-transition

The epithelium to mesenchyme transition (EMT) is a process by which epitheliums lose their cell polarity and cell-cell adhesion, and gain migratory and invasive properties to become mesenchymal stem cells.

EMT is essential for numerous developmental processes including mesoderm formation and neural tube formation. EMT has also been shown to occur in wound healing, in organ fibrosis and in the initiation of metastases for cancer progression.

EMT has also been linked to cancer stem cells and resistance to chemotherapy.

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aimed to evaluate the expression of EMT-related markers in 72 NF-PitNET and 16 non-tumoral pituitaries. To further explore the potential usefulness of medical treatment for NF-PitNET we assessed the expression of somatostatin receptors and dopamine-associated genes.

Results: We found that SNAI1, SNAI2, Vimentin, KLK10, PEBP1, Ki-67 and SSTR2 were associated with invasive NF-PitNET. Furthermore, we found that the EMT phenomenon was more common in NF-PitNET than in GH-secreting pituitary tumors. Interestingly, PEBP1 was overexpressed in recurrent NF-PitNET, and could predict growth recurrence with 100% sensitivity but only 43% specificity. In parallel with previously reported studies, SSTR3 is highly expressed in our NF-PitNET cohort. However, SSTR3 expression is highly heterogeneous among the different histological variants of NF-PitNET with very low levels in silent corticotroph adenomas.

Conclusion: NF-PitNET showed an enhanced EMT phenomenon. SSTR3 targeting could be a good therapeutic candidate in NF-PitNET except for silent corticotroph adenomas, which express very low levels of this receptor. In addition, PEBP1 could be an informative biomarker of tumor regrowth, useful for predictive medicine in NF-PitNET [1)]

An initial in silico data mining in a published ependymoma (EPN) patient series (GSE21687) revealed upregulation of EMT-Transcription factors (EMT-TFs) in tumor samples. Further, quantitative real-time polymerase chain reaction (q-RT-PCR) based gene expression analysis of EMT-TFs in 96 EPNs showed significant up-regulation of SNAI1, SNAI2, ZEB1, and TWIST1 as compared to normal brain, associated with upregulation of CDH2/N-Cadherin and downregulation of CDH1/E-Cadherin. Although this was observed in varying degrees in all clinico-pathological-molecular subgroups of EPNs, it was most evident in supratentorial Ependymoma RELA fusion positive and in posterior fossa ependymomas. Immunohistochemistry performed in 60 of the above cases corroborated with gene expression patterns and immunopositivity for Snail, Slug, Zeb1, and Twist1 was observed in 80%, 80%, 81%, and 63% of all EPNs. Immunopositivity for N-Cadherin and E-Cadherin was observed in 76.6% and 2% cases respectively. Univariate Cox regression analysis showed that low expression of CDH1/E-Cadherin (P=.002) and high expression levels of CDH2/N-Cadherin (P<.001), SNAI1/Snail (P=.023), SNAI2/Slug (P<.001) and ZEB1 (P<.001) to be associated with shorter progression free survival.

Malgulwar et al., report for the first time the existence of EMT- like phenotype in EPNs. These factors could represent new prognostic and therapeutic targets in EPN [2)].

Previous studies have estimated that microRNA (MicroRNA/miR) expression is associated with EMT via the regulation of the expression of target genes. miR 96 has been reported to exhibit a correlation with the EMT process. However, the functional role of miR-96 and its mechanism in glioblastoma multiforme (Glioblastoma) remains to be completely elucidated. The objective of the present study was to investigate the functional role and mechanism of miR-96 in the migration and invasion, in addition to proliferation, apoptosis and cell cycle distribution, of Glioblastoma. In the present study, the results suggested that the introduction of miR-96 significantly inhibited the migration and invasion, in addition to proliferation and cell cycle progression, of Glioblastoma cells and promoted their apoptosis in vitro, leading to the hypothesis that miR-96 may be a potential tumor suppressor. It was subsequently confirmed that astrocyte elevated gene-1 (AEG-1) was a direct target gene of miR-96, using a luciferase assay and reverse transcription-quantitative polymerase chain reaction analysis, in addition to western blotting. miR-96 was observed to downregulate the expression of AEG-1 at the mRNA and protein levels. Notably, AEG-1 may suppress EMT by increasing the expression levels of E-cadherin, an epithelial marker, and decreasing the expression levels of vimentin, a mesenchymal marker. Therefore, it was concluded that miR-96 may impede the EMT process by downregulating AEG-1 in Glioblastoma. Additionally, it was observed that inhibition of AEG-1 led to a similar effect compared with overexpression of miR-96 in Glioblastoma. In conclusion, the results of the present study demonstrated that miR-96 may act as a tumor suppressor by regulating EMT via targeting of AEG-1, suggesting that miR-96 may be a potential biomarker and anticancer therapeutic target for Glioblastoma in the future [3].

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